

CLAIMS

add α_2
add β_2 1. What is claimed is:

- 5 1. A molecularly-mediated cardiac pacemaker construct comprising at least one gene that upregulates heart rate or alters cardiac rhythm suitable for localized gene expression in mammalian cardiac atrial tissue.
2. The cardiac pacemaker of Claim 1 wherein gene expression is localized to the sinoatrial node region of the right atria.
3. The cardiac pacemaker of Claim 2 wherein the gene is selected from the group consisting of: a β_2 AR gene, β_1 AR gene, and G_{α_s} gene.
- 10 4. The cardiac pacemaker of Claim 3 wherein the construct further comprises expression control elements.
5. The cardiac pacemaker of Claim 4 wherein the expression control element directs transient expression.
6. The cardiac pacemaker of Claim 4 wherein the expression control element directs stable expression.
- 15 6. The cardiac pacemaker of Claim 4 wherein the expression control element directs stable expression.
7. The cardiac pacemaker of Claim 6 wherein the expression control element comprises an inducible promoter.
- 20 8. A cellular-based cardiac pacemaker comprising at least one cell transfected or transduced with at least one gene that upregulates heart rate or alters cardiac rhythm.

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9. The cardiac pacemaker of Claim 5 wherein the gene is selected from the group consisting of: a β_2 AR gene, β_1 AR gene, and $G_{\alpha s}$ gene.
10. The cardiac pacemaker of Claim 8 wherein the cell is selected from the group consisting of: a myoblast, a cardiomyocyte, a skeletal muscle myoblast, a fetal or embryonic cardiomyocyte and a cardiac-derived cell line.
11. The cardiac pacemaker of Claim 9 further wherein the cell is isogenic, allogenic, or xenogenic.
12. A method of regulating cardiac pacemaking activity in a mammal by introducing a biologic pacemaker according to Claims 1, 7, 8 or 11 into the sinoatrial node region of a mammalian heart.
13. The method of Claim 12 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.
14. A method of improving cardiac function in senescent heart tissue by introducing a biological pacemaker according to Claim 1, 7, 8 or 11 into an atrial chamber of a mammalian heart.
15. The method of Claim 14 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.
16. The method of Claim 15 wherein the biological pacemaker is a molecular-mediated cardiac pacemaker construct comprising a gene encoding a β_2 -adrenergic receptor, and further wherein the method comprises *in vivo* administration of an adrenergic agonist.
17. The method of Claim 15 wherein the adrenergic agonist is isoproterenol.

18. The method of Claim 14 wherein the biological pacemaker is a cellular-based cardiac pacemaker construct comprising a transfected or transduced cell expressing a β 2-adrenergic receptor and further wherein the method comprises *in vivo* administration of an adrenergic agonist.
- 5 19. The method of Claim 18 wherein the adrenergic agonist is isoproterenol.
20. The method of Claim 18 wherein the transfected or transduced cell comprises at least one fetal or embryonic cardiomyocyte transfected with at least one gene that upregulates heart rate or alters cardiac rhythm.
- 10 21. A method of improving inotropic responsiveness in a mammal with a cardiac conductive tissue dysfunction by introducing a biologic pacemaker according to Claim 1, 6, 7 or 11 into the sinoatrial node region of a mammalian heart.
22. A method of treating a mammal suffering from a heart attack or transient depression of heart rate by delivering to the mammal a transient molecularly-mediated cardiac pacemaker.
- 15 23. A method of permanently regulating cardiac pacemaking activity in a mammal by introducing a cellular-based cardiac pacemaker comprising at least one fetal or embryonic cardiomyocyte transfected or transduced with at least one gene that upregulates heart rate or alters cardiac rhythm.
- 20 24. A method of permanently regulating cardiac pacemaking activity in a mammal by introducing a molecularly-mediated cardiac pacemaker construct comprising at least one gene that upregulates heart rate or alters cardiac

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rhythm suitable for localized stable gene expression in mammalian cardiac atrial tissue.

25. The method of Claim 24 wherein the molecularly-mediated cardiac pacemaker construct comprises an inducible promoter.

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